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10/783,552	02/20/2004	Joseph F. Hicklin	MWS-111RCE3	7454

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EXAMINER
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SKOWRONEK, KARLHEINZ R

ART UNIT	PAPER NUMBER
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1631

MAIL DATE	DELIVERY MODE
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09/13/2010

PAPER

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

<b>Office Action Summary</b>	<b>Application No.</b> 10/783,552	<b>Applicant(s)</b> HICKLIN ET AL.	
	<b>Examiner</b> KARLHEINZ R. SKOWRONEK	<b>Art Unit</b> 1631	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

#### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

#### Status

- 1) ☒ Responsive to communication(s) filed on 16 June 2010.
- 2a) ☐ This action is **FINAL**.                      2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

#### Disposition of Claims

- 4) ☒ Claim(s) 1-39 is/are pending in the application.
- 4a) Of the above claim(s) 6,7,12,13,18,19,24,25,30,31 and 36 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-5,8-11,14-17,20-23,26-29,32-35 and 37-39 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

#### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

#### Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All    b) ☐ Some \*    c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

#### Attachment(s)

- |   |   |
|---|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)         | 4) <input type="checkbox"/> Interview Summary (PTO-413)           |
| 2) <input type="checkbox"/> Notice of Draftperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____                                      |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)         | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date _____   | 6) <input type="checkbox"/> Other: _____                          |

## **DETAILED ACTION**

### ***Continued Examination Under 37 CFR 1.114***

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 16 June 2010 has been entered.

### ***Claim Status***

Claims 1-39 are pending.

Claims 6-7, 12-13, 18-19, 24-25, 30-31, and 36 are withdrawn as being directed to a non-elected invention, the election having been made on 19 March 2007.

Claims 1-5, 8-11, 14-17, 20-23, 26-29, 32-35, and 37-39 have been examined.

Claims 1-5, 8-11, 14-17, 20-23, 26-29, 32-35, and 37-39 are rejected.

### ***Priority***

This application was filed on 20 February 2004 and makes no claims to the benefit of any earlier filed applications.

### ***Claim Objections***

### ***Response to Arguments***

The objection to claims 8, 14, 26, and 32 is withdrawn in view of the amendments to the claims.

### ***Claim Rejections - 35 USC § 103***

***Response to Arguments***

The rejection of claims 1-5 and 20-23 as unpatentable over Sauro et al., in view of Kurata et al., in view of Funhashi et al., and in view of Allen et al. under 35 USC 103(a) has been withdrawn in view of the amendments to the claims. However, upon further consideration, a new ground(s) of rejection is made in view of Sauro et al., in view of Kurata et al., in view of Funhashi et al., and in view of Thalhammer-Reyo.

The rejection of claims 8-11, 14-17, 26-29, and 32-35 as unpatentable over Sauro et al., in view of Kurata et al., in view of Funhashi et al., and in view of Schilling et al. under 35 USC 103(a) has been withdrawn in view of the amendments to the claims. However, upon further consideration, a new ground(s) of rejection is made in view of Sauro et al., in view of Kurata et al., in view of Funhashi et al., and in view of Thalhammer-Reyo.

The rejection of claim 37 as unpatentable over Sauro et al. and in view of Kurata et al. in view of Funhashi et al. and in view of Allen et al. as applied to claims 1-5 and 20-23 above, and further in view of Shannon et al. and in view of Biospice under 35 USC 103(a) is withdrawn in view of the amendments to the claims.

The rejection of claims 38 and 39 as unpatentable over Sauro et al. and in view of Kurata et al. in view of Funhashi et al. and in view of Schilling et al. as applied to claims 1-5 and 20-23 above, and further in view of Shannon et al. and in view of Biospice under 35 USC 103(a) is withdrawn in view of the amendments to the claims.

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The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

The following rejection is necessitated by amendment.

Claims 1-5, 8-11, 14-17, 20-23, 26-29, and 32-35 and are rejected under 35 U.S.C. 103(a) as being unpatentable over Sauro et al., in view of Kurata et al., in view of

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Funhashi et al. (Biosilico, Vol. 1 No. 3, p. 159-162, 2003 November), and in view of Thalhammer-Reyo (WO 96/22575).

The claims are directed to a system, computer-implemented method, and computer program product for improved modeling of a biological system, a biological system being a plurality of chemical reactions, comprising a modeling component with a graphical user interface to generate a model; a simulation engine accepting the model and generating a dynamic behavior for the biologic system; and an analysis environment that interfaces with data acquisition hardware that gathers experimental data and using output to control an experiment.

Sauro et al. show a system, computer-implemented method, and computer program product for improved modeling of a biological system, a biological system being a plurality of chemical reactions, comprising a modeling component with a graphical user interface (GUI) to generate a model; a simulation engine accepting the model and generating a dynamic behavior for the biologic system; and an analysis environment to display the dynamic behavior (figure 11). The system implemented by Sauro et al. integrates several stand-alone programs in a way such that the inputs and outputs of each program can be exchanged with the other programs, i.e. the programs are SBW-compliant or enabled. Sauro et al. shows the integration of the programs of JDesigner, Jarnac, and SBW Meta-tool (p. 365, Applications). In figure 11 of Sauro et al, the elements of modeling component having a GUI providing means for accepting user input via a tool palette to generate a block diagram of a plurality of related chemical reactions that make a biological system. The figure also depicts an analysis

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environment displaying the dynamic behavior of the biological system, and a simulation engine. The system of Sauro et al. integrates several different programs as components and facilitates the intercommunication of the programs to provide a dynamic, high performance framework for modeling biological systems and reaction pathways (p. 355). Figure 12 shows that in addition to depicting the model graphically, the model is also displayed as a table. Figure 12 shows screen shot of JDesigner interfaced with METATOOL. Sauro et al. shows JDesigner acts as a model editor from which users can initiate simulation and METATOOL analysis (p. 368). In the lower left portion of figure 12, the tabular view of METATOOL displays the modes, sets of enzymes working together at steady state to construct a plausible subpathways, of the reactions representative of the model displayed in graphical format in the center of figure 12. Thus, Sauro et al. shows the adaptation of the tabular view to receive user commands and input to construct the model. Sauro et al. show that the dynamic behavior of the system is modeled using a stochastic computational model (p 355 and 364). Sauro et al. also shows that models are entered in the form of a script stored in SBML level 1. Sauro et al. shows the JARNAC tool is a script based simulation tool using models stored in SBML level 1 (p. 366). The SBML script is another tabular form of a model.

Sauro et al. does not explicitly show the display of one or more reactions in tabular form.

Kurata et al. shows a computational system for the modeling of biochemical reaction networks. Kurata et al. shows that a portion of the model is displayed in tabular form and the tables have at least one chemical reaction (figure 3). Kurata et al. shows

the benefit of the GUI is it allows one to draw and describe a large-scale map of molecular networks (p. 4076, col. 1). Kurata et al suggests the CADLIVE system not only constructs a large-scale map of complicated signal transduction pathways based on the information provided by molecular biology, but also has the capability to map the heterogeneous experimental data derived from DNA microarrays and proteomics studies on a biochemical network of interest (4084, col. 1).

Sauro et al. in view of Kurata et al. do not show a reaction table with a plurality of reactions and a species table that depicts at least one initial condition and amount of material.

Funhashi et al. shows in figure 1 table of reactions (bottom left) with a plurality of reaction and a table of species (bottom right) with at least an initial condition and an amount of a starting material. The relevant portion of figure 1 is included here for clarity.

name	id	name	rate	time	species	amount	position
STATE_TRANSITION	r1	state	rate	time	s20	s11	s20
STATE_TRANSITION	r2	state	rate	time	s11	s12	
STATE_TRANSITION	r3	state	rate	time	s11	s13	
STATE_TRANSITION	r4	state	rate	time	s11	s14	
STATE_TRANSITION	r5	state	rate	time	s11	s15	
STATE_TRANSITION	r6	state	rate	time	s11	s16	

  

name	id	name	rate	time	species	amount	position
PROTEIN	s1	protein	rate	time	s1	s1	s1
PROTEIN	s2	protein	rate	time	s2	s2	s2
PROTEIN	s3	protein	rate	time	s3	s3	s3
PROTEIN	s4	protein	rate	time	s4	s4	s4
PROTEIN	s5	protein	rate	time	s5	s5	s5
PROTEIN	s6	protein	rate	time	s6	s6	s6

Funhashi et al. shows the standardized model description enhances the portability of the models between software tools (p. 160, col. 1).

Thalhammer-Reyo shows methods and systems for simulating biochemical processes. Thalhammer-Reyo shows that simulation system or engine is interfaced and integrated with an experiment (p. 10). In the case of Thalhammer-Reyo the experiment is a biological reactor or reactor. Thalhammer-Reyo shows that a data acquisition hardware is monitored by a monitoring interface that acts as bridge to pass information



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from the experiment to the model (p. 10). Thalhammer-Reyo shows the model transmits information to controller hardware to regulate the operation of the experiment (p. 10).

Thalhammer-Reyo shows the system models the dynamic behavior of the processes of the experiment and involves any number of variable to be monitored, including those measured and monitored in the experiment and those simulated and monitored in the model, which are both used as inputs for an inference engine to be compared against each other or other specified values and which meeting the specified conditions (a predetermined amount) trigger actions that result in the control of the experiment (p. 11). Thalhammer-Reyo shows the system advantageously provides a means to build detailed mechanistic models of the complex systems involved; and to use inference methods that integrate the simulation of virtual models with inputs from monitoring devices to allow for the intelligent control of the operation of complex systems (p. 4).

It would have been obvious to one of ordinary skill in the art at the time of invention to modify the biological simulation system of Sauro et al. with the display of Kurata et al. because Kurata et al. shows that a benefit of the display is it allows one to draw and describe a large scale map of molecular networks. It would have been further obvious to one of skill in the art at the time of invention to modify the biological simulation of Sauro et al. in view of Kurata et al. with the tabular views of Funhashi et al. because Funhashi et al. shows standardized model description enhances the portability of the models between software tools. It would have been further obvious to one of ordinary skill in the art at the time of invention to modify the biological simulation system of Sauro et al. with the display of Kurata et al. and the editing of reaction and species

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via a tabular view of Funhashi et al. because all the claimed elements were known, in the prior art, and one skilled in the art could have combined the elements as claimed by known methods with no change in their respective functions, and the combination would have yielded nothing more than predictable results to one of ordinary skill in the art at the time of the invention. It would have been further obvious to one of ordinary skill in the art at the time of invention to modify the biological simulation system of Sauro et al. using the display of Kurata et al. and the editing of reaction and species via a tabular view of Funhashi et al. with the interfacing of data acquisition hardware and control hardware for an experiment of Thalhammer-Reyo because Thalhammer-Reyo shows the system advantageously provides a means to build detailed mechanistic models of the complex systems involved; and to use inference methods that integrate the simulation of virtual models with inputs from monitoring devices to allow for the intelligent control of the operation of complex systems.

### ***Response to Arguments***

Applicant's arguments filed 16 June 2010 have been fully considered but they are not persuasive. Applicant argues that Sauro et al., in view of Kurata et al., and in view of Funhashi et al. fails to show and an analysis environment that interfaces with data acquisition hardware that gathers experimental data and uses the output to control a property of an experiment. This is not persuasive because Thalhammer-Reyo shows an analysis environment or inference engine that interfaces with data acquisition hardware to gather experimental data and uses the output to control properties of the experiment (p. 10). Applicant argues that Sauro et al., in view of Kurata et al., and in view of

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Funhashi et al. fail to show an indication when the data acquired and the model are compared and are greater than a predetermined amount. Thalhammer-Reyo shows that a comparison between the data acquired and the data from the model is determined and analyzed with respect to a threshold (p. 11).

The following rejection is necessitated by amendment.

Claim 37-39 is rejected under 35 U.S.C. 103(a) as being unpatentable over Sauro et al. and in view of Kurata et al. in view of Funhashi et al. and in view of Thalhammer-Reyo as applied to claims 1-5, 8-11, 14-17, 20-23, 26-29, and 32-35 above, and further in view of Shannon et al. (Genome Research, Vol. 13, p. 2498-2504, 2003) and in view of Biospice (Presentation of Biospice, DARPA BioComp, May 2002).

Claims 37-39 are directed to embodiments in which user annotations are displayed in a column in a table and in a location close to an element in the graphical view.

Sauro et al. and in view of Kurata et al. in view of Funhashi et al. and in view of Thalhammer-Reyo as applied to claims 1-5, 8-11, 14-17, 20-23, 26-29, and 32-35 above show a computational system for modeling chemical reactions.

Sauro et al. and in view of Kurata et al. in view of Funhashi et al. and in view of Thalhammer-Reyo does not explicitly show user annotations are displayed in a column view and in a location close to an element in the graphical view.

Shannon et al. shows a system for simulating biochemical reactions and interactions. Shannon et al. shows that data is integrated with the graph model using

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attributes (p. 2499, col. 2). Shannon et al. shows that attribute values may assume any type (e.g., text strings, discrete or continuous numbers, URLs, or lists) and are either loaded from a data repository or generated dynamically within a session reading on user annotations (p. 2499, col. 2). Shannon shows in figure 1a table with annotations in a column view. Shannon et al. shows that it is possible to have many levels of annotation all active and on display at the same time, each as a different attribute on the nodes or edges of interest (p. 2500, col. 1-2). Shannon et al. shows that annotations are transferred on to the nodes and edges (p. 2500, col. 1). Shannon et al. shows that by visually superimposing molecular states on the interaction pathways hypothesized to regulate those states, attribute-to-visual mappings directly connect observed data to an underlying model (p. 2500, col. 2).

Biospice shows annotations are localized close to elements in the graphical view (p. 32).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to modify the system for modeling biochemical reactions of Sauro et al. and in view of Sauro et al. and in view of Kurata et al. in view of Funhashi et al. and in view of Thalhammer-Reyo as applied to claims 1-5, 8-11, 14-17, 20-23, 26-29, and 32-35 above with annotations in a column and localized close to elements in the graphical view as shown by Shannon et al. and Biospice because all the claimed elements were known, in the prior art, and one skilled in the art could have combined the elements as claimed by known methods with no change in their respective functions, and the combination would have yielded nothing more than predictable

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results to one of ordinary skill in the art at the time of the invention. It would have been obvious to one of ordinary skill in the art at the time the invention was made to modify the system for modeling biochemical reactions of Sauro et al. and in view of Kurata et al. in view of Funhashi et al. and in view of Thalhammer-Reyo as applied to claims 1-5 and 20-23 above with annotations in a column and localized close to elements in the graphical view as shown by Shannon et al. and Biospice because Shannon et al. shows by visually superimposing molecular states on the interaction pathways hypothesized to regulate those states, attribute-to-visual mappings directly connect observed data to an underlying model.

### ***Conclusion***

Any inquiry concerning this communication or earlier communications from the examiner should be directed to KARLHEINZ R. SKOWRONEK whose telephone number is (571)272-9047. The examiner can normally be reached on 8:00am-5:00pm Monday-Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Marjorie Moran can be reached on (571) 272-0720. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/KARLHEINZ R SKOWRONEK/  
Primary Examiner, Art Unit 1631

11 September 2010